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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,838	06/24/2003	Birthe Lykkegaard Hansen	6423.404-US	9325

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EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/602,838	HANSEN ET AL.	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,7,10-19,21-26 and 29-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,10-19,21-26 and 29-31* is/are rejected.

7)☒ Claim(s) *10 and 12-13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/ are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment after Non-final filed November 27, 2007 is acknowledged. Claims 5, 8-9, 20, 27-28 and 32-37 have been cancelled. Claims 1-4, 6-7, 10-19, 21-26 and 29-31 are pending in this application, and these claims are examined on the merits in this office action.

Withdrawn Rejections

1. Rejection of claims 1-4, 6-7, 10-19, 21-26 and 29-31 under 35 U.S.C. 112, second paragraph is hereby withdrawn due to Applicant's amendment to the claims.

2. Rejection of claims 1-4, 6-7, 9-16, 21-23, 25-26 and 29-31 and claims 1-4, 6-7, 10-19, 21-26 and 29-31 under 35 U.S.C. 102(b) are hereby withdrawn due to Applicant's arguments and amendment to the claims.

3. Rejection of claim 8 under 35 U.S.C. 103 is hereby withdrawn due to Applicant's cancellation of claim 8.

Obviousness Double Patenting Rejection and Terminal Disclaimer

3. Applicants stated that the Applicants will file a terminal disclaimer disclaiming any terms of claims 1, 7, 10-12, 14-15, 17-19 and 24 issuing from the present application beyond the term of any patents that issue from co-pending application 10/602340. Until a properly executed terminal disclaimer is filed and approved by the Office, Obviousness Double Patenting rejection is maintained.

New Objection

4. Claims 10 and 12-13 are objected to under 37 CFR 1.75©, as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 10 recites "a composition according to claim 1, further comprising (v) a tonicity modifying agent." However, claim 1 recites that "calcium salt in a concentration of at least 200 mM, such that the composition is hypertonic." This phrase implies that calcium salt is the tonicity modifying agent. Therefore, claims 10 and 12-13 do not further limit claim 1.

New Rejection

35 U.S.C. 112, 2nd

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 10 and 12-13 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 10 recites "a composition according to claim 1, further comprising (v) a tonicity modifying agent." However, claim 1 recites that "calcium salt in a concentration of at least 200 mM, such that the composition is hypertonic." This phrase implies that calcium salt is the tonicity modifying agent. Therefore, it is unclear how there could be two tonicity modifying agent.

Rejection-35 U.S.C. 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-4, 6-7, 10-19, 21-26 and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over The Medicine Catalogue (Laegemiddel Kataloget), of record, in

view of Pingel et al (US Patent No. 6903069) and Johannessen et al (WO 01/82943) and Perez Garcia (US Patent No. 2145869).

12. The instant claims are drawn to a liquid, aqueous composition comprising a factor VII polypeptide, an agent for keeping pH from about 5.5 to about 7.0, and a calcium salt in concentration of at least 200 mM.

13. The Medicine Catalogue discloses a composition with recombinant coagulation factor VIIa, with 1.5 mg calcium chloride, 1.3 mg glycinglycine, 30 mg mannitol, 3.0 mg sodium chloride, and 0.1 mg polysorbate 80 per ml, wherein the composition has a pH of 5.4 to 6.0 (see Dispensed in the form on). This means that 13.51 mM of $CaCl_2$ is in the formulation per 1 ml of solution. For sodium chloride (MW 59 g/mol) and using 3 mg and dissolving in 1 ml of solution, this yields 50 mM of NaCl concentration. The Medicine Catalogue further teaches that factor VII polypeptide concentration is 1.2, 2.4 or 4.8 mg per ml of solution. When the injection fluid is prepared, this means that 0.6 mg/ml (for 1.2 mg/2ml), 1.2 mg/ml (for 2.4 mg/2ml), 2.4 mg/ml (for 4.8 mg/2ml) etc will be prepared. This reads on claim 29. Furthermore, the reference teaches that the preparations are dissolved in varying amounts of sterile water, and that they are administered by a bolus injection (see Suggest dosage). This reads on claims 30-31. Additionally, since different amounts of sterile water are used to reconstitute the composition while the mass of the excipients does not change, the concentrations of the excipients will be commensurate with instant claims. For example, 30 mg of mannitol (MW 182.17 g/mol) used in The Medicine Catalogue, which meets the limitation of claim 11 is found to be 82 mM for 2 ml, 41 mM for 4 ml and 21 mM for 8 ml of sterile water,

meeting the limitations of claims 12-13. It is noted that claims 1-4, 6-7, 10-19, 21-26 and 29-31 have been rejected over the prior art, even though the reference does not disclose exact pH range and exact amount (range) as claimed. However, the claims utilize the term "about" when discussing the pH and the amount. The term "about" allows for some tolerance in the ranges disclosed. In *In re Ayers*, the Federal Circuit held that "at least about 10%" was anticipated by a reference that disclosed "about 8%" because the term "about" allowed for some tolerance. In re Ayers, 154 F.2d 182, 185 (Fed. Cir. 1946). Similarly, in Johnson and Johnson v. W.L. Gore & Associates, Inc., the Court allowed for "about 1.2" to be inclusive of 1.0. See Johnson and Johnson v. W.L. Gore & Associates, Inc., 436 F.Supp. 704, 728-729 (Fed. Cir. 1977). Although about has never been confined to specific percentage of variability, the Johnson and Johnson decision at least implies that 16% variability is permissible when "about" is used (1.0/1.2 = ~16.6% variability). Thus, the term "about" implicitly discloses some variability even though the specification may not literally cite this variability. Therefore, The Medicine Catalogue meets the limitations of claims 1-4, 6-7, 10-19, 21-26 and 29-31. The difference between the reference and the instant claims is that the reference does not teach calcium salt in the concentration of at least 200 mM.

15. However, Johannessen et al disclose factor VIIa for the manufacture of a medicament for treatment of a condition affectable by Factor VIIa, medicament being for subcutaneous, intra-muscular or intradermal administration...shows a prolonged biological half-life (see abstract). Calcium or other divalent metal ions, is necessary for the maintenance of the FVIIa activity...calcium chloride...in an amount of more than

0.15 mg/ml (see p. 19, lines 25-28). Additionally, the reference discloses that the medicament may also comprise salt in order to five an isotonic solution, e.g. NaCl, KCl...in an amount of more than 1.0 mg/ml (see p. 9, lines 22-24). The reference further discloses that preservatives such as benzyl alcohol, phenol, sorbic acid, parabens, and chlorocresol may be added (see p. 10, lines 1-14). Please note that the instant specification discloses that factor VII polypeptides include factor VIIa (see paragraph [0017]) and that factor VII polypeptide is human factor VIIa, recombinant human factor VIIa, a factor VII-related polypeptide, factor VII sequence variant (see paragraph [0043]).

16. Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of The Medicine Catalogue and Johannessen to produce a liquid, aqueous composition comprising factor VII polypeptide, since The Medicine Catalogue and Johannessen teach the formulation of Factor VII. Therefore, one of ordinary skilled in the art would have been motivated to optimize the $CaCl_2$ concentration, since Johannessen indicates that $CaCl_2$ maintains the FVIIa activity, and is required in an amount more than 0.15 mg/ml. The MPEP states the following: Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. *"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."* In re Aller, *220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)* (Claimed process which was performed at a temperature between 40°C and 80°C

and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("*The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.*"); *In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969)* (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Therefore, there is a reasonable expectation of success, since having a $CaCl_2$ concentration in an amount more than 0.15 mg/ml maintains FVIIa activity, optimizing the concentration would stabilize FVIIa activity. Since artisans are always trying to optimize the peptide stability and maintain peptide activity, by optimizing the $CaCl_2$ concentration in an amount more than 0.15 mg/ml, one would at least expect a more stable liquid formulation.

Conclusion

17. Applicant's amendment necessitated the new ground(s).of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). No claims are allowed.

18. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 5:30 AM to 3:00 PM.

20. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

21. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Julie Ha
Patent Examiner
AU 1654

2/3/09
ANISH GUPTA
PRIMARY EXAMINER